<u>Remarks:</u>

Claims 1 to 15, 17 to 26, and 28 to 30 are pending.

Claims 1, 4, and 21 have been amended for clarification as discussed below.

<u>Indefiniteness Rejection</u>

Claims 1-15, 17-26, and 28-30 are rejected under 35 USC 112, second paragraph, as being indefinite. In particular, the Office Action identifies certain limitations recited in claims 1, 4 and 21 as confusing, and states that the other claims are rejected due to their dependency from claim 1, 4 or 21.

Specifically, the Office Action states that the expression "wherein the weights used to weight said deviates are determined with a constraint that said weights associated with sets of said data having like genetic data are the same" recited in claims 1 and 21 "could be interpreted as an active method step" or "simply as a further limitation of the weights". Claims 1 and 21 have been amended to recite "<u>determining</u> the weights used to weight said deviates with a constraint [...]" for clarification.

The Office Action also states that the clause "that said weights associated with sets of said data having like genetic data are the same" is unclear as it has two possible interpretations: (1) "the weights are the same" and (2) "the sets of data are the same." The applicant respectfully disagrees. Under interpretation (2), the phrase "said weights associated with" would serve no purpose and render the entire clause grammatically incorrect. Thus, the only possible interpretation is interpretation (1).

The Office Action further states that the expression "data having <u>like</u> genetic data like genetic data" (emphasis added) recited in claim 4 is unclear as the expression "like genetic data" is repeated. The applicant respectfully disagrees. The above expression does not appear in claim 4. Rather, claim 4 recites "<u>sets of data having genetic data</u> like genetic data obtained

from said member". The meaning of that expression is clear in context – the genetic data in each of the selected sets and the genetic data obtained from the member are alike.

The Office Action further states that the expression "data having <u>like</u> genetic data like genetic data" (emphasis added) is recited in claim 4 and is unclear as "like genetic data" . The applicant respectfully disagrees, as claim 4 does not recite the above expression. Rather, claim 4 recites "<u>sets of data having genetic data</u> like genetic data obtained from said member", the meaning of which is believed to be clear in context.

The Office Action also states that the term "corresponding weight" in claim 4 is unclear. The word "corresponding" has been deleted for clarification.

In view of the above, Applicant respectfully requests withdrawal of the indefiniteness rejections to claims 1, 4 and 21, and claims dependent directly or indirectly therefrom.

The Office Action fails to provide any reason for the indefiniteness rejection of claims 28-30, none of which is dependent directly or indirectly from any of claims 1, 4 and 21. Thus, Applicant also respectfully requests withdrawal of the indefiniteness rejections to claims 28-30.

<u>Rejections under 35 USC 103(a)</u>

In the Office Action, claims 1-6, 9-11, 13-15, 17-21, and 28-30 are rejected under 35 USC 103(a) as obvious having regard to Parzen, in view of Shattuck-Eidens et al. and Cleveland. Dependent claims 7, 8, 12, and 22-26 are also rejected under 35 USC 103(a) as obvious having regard to Parzen, in view of Shattuck-Eidens et al. and Cleveland, and additionally in view of Kooperberg et al. and Hu. et al. Applicant respectfully traverses these rejections for at least the following reasons.

Independent Claim 28 recites "calculating a deviate from an indicator of a disease status of each member by a predicted risk for that member, predicted <u>using that model and non-genetic data associated with that member</u>, and a sum of weighted

deviates, each deviate weighted by <u>a weight reflecting genetic data associated with that member for whom that deviate is calculated</u>" (emphasis added).

As acknowledged in the Office Action, Parson discloses a global goodness-of-fit test statistic for a Cox regression model, using data of "non-genetic risk factors," but does not disclose or suggest the use of a combination of both genetic and non-genetic risk factors in the fitting.

Cleveland discloses a method for optimizing models based on weighted regression. Cleveland does not disclose or suggest any method of predicting disease risk, let alone a method of predicting disease risk based on both genetic and non-genetic data (risk factors).

The Office Action relies on Shattuck-Eidens et al. for disclosing "a statistical model for predicating disease risk using a plurality of genetic risk factors" (p7, paragraph 3 of the Office Action). However, careful review of Shattuck-Eidens et al. reveals that it discloses a method of modeling of risk factors for calculating the "probability of a patient carrying a deleterious BRCA1 mutation" where the factors considered for assessing the risk are the following:

- "patient disease status"
- "Patient age at first diagnosis of breast or ovarian cancer"
- "Patient ethnicity with respect to Ashkenazi descent"
- "Number of relatives affected with breast cancer, but not ovarian cancer"
- "Number of relatives affected with ovarian cancer, but not breast cancer"
- "Number of relatives affected with both breast cancer and ovarian cancer"
(see p. 1243, col. 3 and p. 1244, and also Table 6, of Shattuck-Eidens et al.).

The Office Action appears to assert that the above factors are "genetic risk factors." The Applicant respectfully disagrees. As discussed in the present application at paragraph [0035] (paragraph [0038] in the published application), "age", "medical history of certain diseases", "race", and "family history of the disease" are all <u>non-genetic</u> factors. Thus, all of the factors considered for assessing the risk of carrying a mutation in Shattuck-Eidens et al., as listed above, are non-genetic factors, not genetic risk factors.

Kooperberg et al. and Hu. et al. also fail to cure the above defect of Parzen, Shattuck-Eidens et al., and Cleveland.

Consequently, it is respectfully submitted that the cited references, either alone or in combination, fail to disclose all of the elements recited in claim 28, and the Office Action has failed to establish a *prima facie* case of obviousness for claim 28.

Likewise, it is respectfully submitted that the Office Action has failed to establish a *prima facie* case of obviousness for any of claims 1-15, 17-26, and 29-30 for the same reasons.

Withdrawal of the rejections under 35 USC 103(a) is thus respectfully requested.

It is additionally noted that, as in the previous Office Actions, the current Office Action has failed to point to any specific disclosure in the cited references for disclosing or suggesting, for example, the combined features of predicting risk for a member of the population using a model and non-genetic data associated with that member, but weight the deviate for that member by a weight reflecting genetic data associated with that member, in combination with other features recited in claim 28. It is reiterated that the subject matter claimed in the present invention patentably distinguishes over the cited art, not merely because both genetic data and non-genetic data are used, but also because genetic data and non-genetic data are used in different, specific manners as recited in the claims. It is submitted that the cited references, either alone or in combination, fail to disclose or suggest the specific method of using both genetic and non-genetic data to predict disease risk claimed in the present application.

In view of the foregoing, favourable reconsideration of the application is respectfully requested.

Respectfully submitted,

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